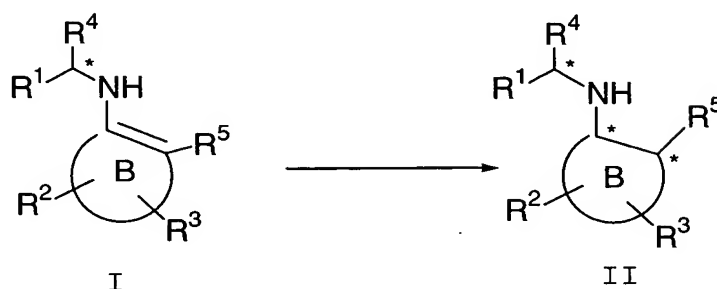


WHAT IS CLAIMED IS:

1. A process of forming a compound of formula II, comprising:



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(a) contacting a compound of formula I with sub-stoichiometric amounts of a platinum catalyst in the presence of a solvent under hydrogen pressure and super-stoichiometric amounts of an acid; wherein:

the platinum catalyst is platinum on charcoal (Pt/C) or Adam's catalyst
 10 (platinum(IV)-dioxide, PtO₂);

the solvent is a protic solvent or a mixture of protic and aprotic solvents;

ring B is a 4-7 membered non-aromatic carbocyclic or heterocyclic ring
 consisting of: carbon atoms, 0-3 carbonyl groups, 0-3 double bonds, and 0-2 ring
 heteroatoms selected from O, N, NR⁶, and S(O)_p, provided that ring B contains other
 15 than a S-S, O-O, or S-O bond;

R¹ is Q, -C₁₋₆ alkylene-Q, -C₂₋₆ alkenylene-Q, or -C₂₋₆ alkynylene-Q;

R² is Q, -C₁₋₆ alkylene-Q, -C₂₋₆ alkenylene-Q, -C₂₋₆ alkynylene-Q,
 -(CR^aR^{a1})_rO(CR^aR^{a1})_s-Q, -(CR^aR^{a1})_rNR^a(CR^aR^{a1})_s-Q, -(CR^aR^{a1})_rC(O)(CR^aR^{a1})_s-Q,
 -(CR^aR^{a1})_rC(O)O(CR^aR^{a1})_s-Q, -(CR^aR^{a1})_rC(O)NR^aR^{a1},
 20 -(CR^aR^{a1})_rC(O)NR^a(CR^aR^{a1})_s-Q, -(CR^aR^{a1})_rS(O)_p(CR^aR^{a1})_s-Q, or
 -(CR^aR^{a1})_rSO₂NR^a(CR^aR^{a1})_s-Q;

Q is, independently at each occurrence, H, a C₃₋₆ carbocycle substituted with 0-3
 R^d, or a 5-10 membered heterocycle consisting of: carbon atoms and 1-4 heteroatoms
 selected from the group consisting of N, O, and S(O)_p, and substituted with 0-3 R^d;

25 R³ is H, Cl, F, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, -(CH)_r-phenyl substituted
 with 0-3 R^d, or -(CH)_r-5-6 membered heterocycle consisting of: carbon atoms and 1-4

heteroatoms selected from the group consisting of N, O, and S(O)_p, and substituted with 0-3 R^d;

alternatively, when R² and R³ are attached to the same carbon atom, they form a 3-8 membered carbocyclic or heterocyclic spiro ring C substituted with 0-2 R^c and consisting of carbon atoms, 0-4 heteroatoms selected from O, N, and S(O)_p, and 0-2 double bonds, provided that ring C contains other than a S-S, O-O, or S-O bond;

alternatively, when R² and R³ are attached to adjacent carbon atoms, together with the carbon atoms to which they are attached they form a 5-7 membered carbocyclic or heterocyclic ring D substituted with 0-2 R^c and consisting of carbon atoms, 0-2 heteroatoms selected from the group consisting of N, O, and S(O)_p, and 0-3 double bonds;

R⁴ is H, C₁₋₆ alkyl substituted with 0-1 R^b, C₂₋₆ alkenyl substituted with 0-1 R^b, or C₂₋₆ alkynyl substituted with 0-1 R^b;

R⁵ is -CH₂OR^a or -C(O)OR^a;

R⁶ is Q, -C₁₋₆ alkylene-Q, -C₂₋₆ alkenylene-Q, -C₂₋₆ alkynylene-Q, -(CR^aR^{a1})_rC(O)(CR^aR^{a1})_s-Q, -(CR^aR^{a1})_rC(O)-C₂₋₆ alkenylene-Q, -(CR^aR^{a1})_rC(O)O(CR^aR^{a1})_s-Q, -(CR^aR^{a1})_rC(O)NR^aR^{a1}, -(CR^aR^{a1})_rC(O)NR^a(CR^aR^{a1})_s-Q, -(CR^aR^{a1})_rS(O)_p(CR^aR^{a1})_s-Q, or -(CR^aR^{a1})_rSO₂NR^a(CR^aR^{a1})_s-Q;

R^a is, independently at each occurrence, H, C₁₋₆ alkyl, phenyl, or benzyl;

R^{a1} is, independently at each occurrence, H or C₁₋₆ alkyl;

R^{a2} is, independently at each occurrence, C₁₋₆ alkyl, phenyl, or benzyl;

R^b is, independently at each occurrence, C₁₋₆ alkyl substituted with 0-1 R^c, -OR^a, -SR^a, Cl, F, Br, I, =O, CN, NO₂, -NR^aR^{a1}, -C(O)R^a, -C(O)OR^a, -C(O)NR^aR^{a1}, -C(S)NR^aR^{a1}, -NR^aC(O)NR^aR^{a1}, -OC(O)NR^aR^{a1}, -NR^aC(O)OR^a, -S(O)₂NR^aR^{a1}, -NR^aS(O)₂R^{a2}, -NR^aS(O)₂NR^aR^{a1}, -OS(O)₂NR^aR^{a1}, -S(O)_pR^{a2}, CF₃, -CF₂CF₃, -CHF₂, -CH₂F, or phenyl;

R^c is, independently at each occurrence, H, C₁₋₄ alkyl, -OR^a, Cl, F, Br, I, =O, CF₃, CN, NO₂, -C(O)R^a, -C(O)OR^a, -C(O)NR^aR^a, or -S(O)_pR^a;

R^d is, independently at each occurrence, C₁₋₆ alkyl, -OR^a, Cl, F, Br, I, =O, CN, NO₂, -NR^aR^{a1}, -C(O)R^a, -C(O)OR^a, -C(O)NR^aR^{a1}, -C(S)NR^aR^{a1}, -NR^aC(O)NR^aR^{a1},

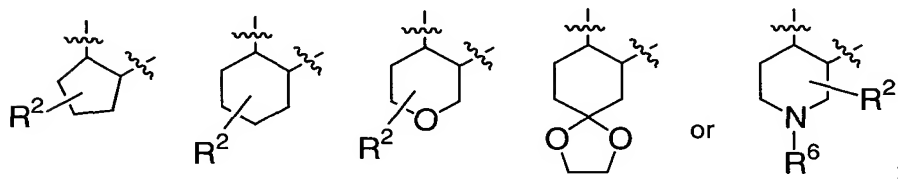
-OC(O)NR^aR^{a1}, -NR^aC(O)OR^a, -S(O)₂NR^aR^{a1}, -NR^aS(O)₂R^{a2}, -NR^aS(O)₂NR^aR^{a1}, -OS(O)₂NR^aR^{a1}, -S(O)_pR^{a2}, CF₃, -CF₂CF₃, C₃₋₁₀ carbocycle, or a 5-6 membered heterocycle consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)_p;

5 p, at each occurrence, is selected from 0, 1, and 2;

r, at each occurrence, is selected from 0, 1, 2, 3, and 4; and

s, at each occurrence, is selected from 0, 1, 2, 3, and 4.

10 2. A process according to Claim 1, to form a compound of formula II, wherein:
ring B is:



R¹ is phenyl substituted with 0-3 R^d;

R² is Q, -C₁₋₆ alkylene-Q, -C₂₋₄ alkenylene-Q, -C₂₋₄ alkynylene-Q,

15 -C(O)(CR^aR^{a1})_s-Q, -C(O)O(CR^aR^{a1})_s-Q, -C(O)NR^aR^{a1}, -C(O)NR^a(CR^aR^{a1})_s-Q, -S(O)_p(CR^aR^{a1})_s-Q, or -SO₂NR^a(CR^aR^{a1})_s-Q;

Q is, independently at each occurrence, H, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, tetrahydro-2H-pyran-4-yl, or phenyl substituted with 0-2 R^d;

R⁴ is C₁₋₄ alkyl;

20 R⁵ is -CH₂OR^a or -C(O)OR^a;

R⁶ is Q, -C₁₋₆ alkylene-Q, -C₂₋₄ alkenylene-Q, -C₂₋₄ alkynylene-Q,

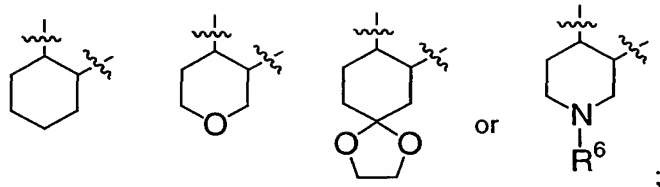
-C(O)(CR^aR^{a1})_s-Q, -C(O)O(CR^aR^{a1})_s-Q, -C(O)NR^aR^{a1}, -C(O)NR^a(CR^aR^{a1})_s-Q, -S(O)_p(CR^aR^{a1})_s-Q, or -SO₂NR^a(CR^aR^{a1})_s-Q; and

R^d is, independently at each occurrence, C₁₋₆ alkyl, -OR^a, Cl, F, Br, =O,

25 -NR^aR^{a1}, -C(O)R^a, -C(O)OR^a, -C(O)NR^aR^{a1}, -S(O)₂NR^aR^{a1}, -NR^aS(O)₂R^{a2}, -S(O)_pR^{a2}, CF₃ or phenyl.

3. A process according to Claim 2, to form a compound of formula II, wherein:

ring B is:



R^1 is phenyl;

5 R^4 is C_{1-4} alkyl;

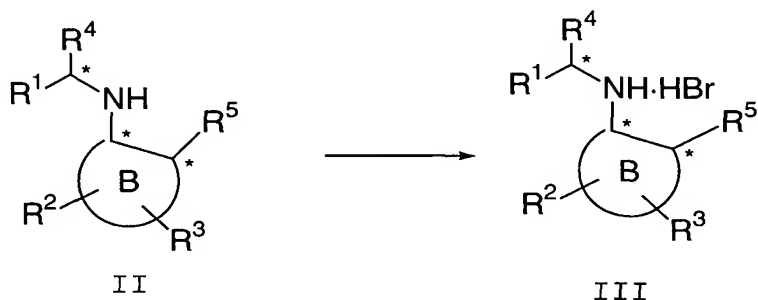
R^5 is $-C(O)OR^a$;

R^6 is H, methyl, isopropyl, butyl, isobutyl, neopentyl, allyl, 3-butenyl, 2-propynyl, 2-butyryl, 3-butyryl, acetyl, t-butylcarbonyl, 4-pentenyl, t-butoxycarbonyl, methoxycarbonyl, methylsulfonyl, propylsulfonyl, isopropylsulfonyl, butylsulfonyl, 10 phenyl, 4-F-phenyl, 4-methoxy-phenyl, cyclopropylmethyl, cyclopentyl, and tetrahydro-2H-pyran-4-yl; and

R^a is C_{1-4} alkyl.

15 4. A process according to Claim 1, further comprising:

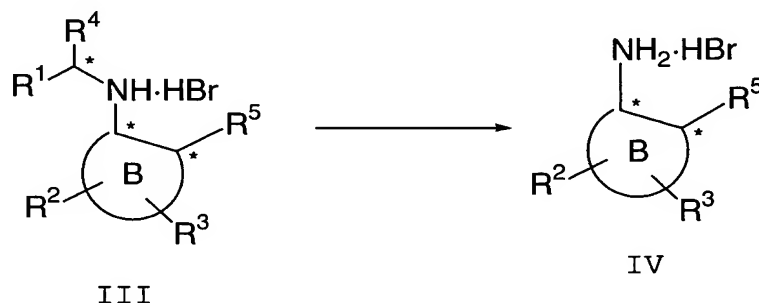
(b) contacting the product from (a) with a hydrogen bromide solution in an acid to yield compound III;



20

5. A process according to Claim 2, further comprising:

(c) contacting the product from (b) with palladium on charcoal catalyst (Pd/C) in the presence of a solvent under hydrogen pressure to yield compound IV; wherein the solvent is a protic solvent or a mixture of protic and aprotic solvents;



- 5
6. A process according to Claim 1, wherein in (a):
the protic solvent is selected from: methanol, ethanol, propanol, 2-butanol, water,
10 ethylene glycol, propylene glycol, and butylene glycol; and
the aprotic solvent is selected from: tetrahydrofuran, dibutyl ether, 1,2-dimethoxyethane, dimethoxymethane, and diethoxymethane.
- 15 7. A process according to Claim 6, wherein in (a):
the protic solvent is selected from: methanol, ethanol, propanol, and 2-butanol;
and
the aprotic solvent is selected from: tetrahydrofuran and dimethoxymethane.
- 20 8. A process according to Claim 7, wherein in (a):
the protic solvent is methanol; and
the aprotic solvent is tetrahydrofuran.
- 25 9. A process according to Claim 1, wherein in (a):
the hydrogen pressure is 10 to 400 psig.

10. A process according to Claim 9, wherein in (a):
the hydrogen pressure is 100 to 300 psig.
- 5 11. A process according to Claim 10, wherein in (a):
the hydrogen pressure is 250 psig.
12. A process according to Claim 1, wherein in (a):
10 the acid is selected from: formic acid, acetic acid, chloroacetic acid,
dichloroacetic acid, trichloroacetic acid, trifluoroacetic acid, propionic acid, isobutyric
acid, hydrochloric acid, and sulfuric acid.
- 15 13. A process according to Claim 12, wherein in (a):
the acid is acetic acid.
14. A process according to Claim 2, wherein in (b):
20 the acid is acetic acid or formic acid.
15. A process according to Claim 14, wherein in (b):
the acid is acetic acid.
25
16. A process according to Claim 3, wherein in (c):
the protic solvent is selected from: methanol, ethanol, propanol, 2-butanol, water,
ethylene glycol, propylene glycol, and butylene glycol; and
30 the aprotic solvent is selected from: tetrahydrofuran, dibutyl ether, 1,2-
dimethoxyethane, dimethoxymethane, and diethoxymethane.
17. A process according to Claim 16, wherein in (c):

the protic solvent is selected from: methanol, ethanol, propanol, and 2-butanol;
and

the aprotic solvent is selected from: tetrahydrofuran and dimethoxymethane.

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18. A process according to Claim 17, wherein in (c):

the protic solvent is methanol; and

the aprotic solvent is tetrahydrofuran.

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19. A process according to Claim 3, wherein in (c):

the hydrogen pressure is 20 to 300 psig.

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20. A process according to Claim 19, wherein in (c):

the hydrogen pressure is 50 to 150 psig.

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21. A process according to Claim 20, wherein in (c):

the hydrogen pressure is 100 psig.

25

22. A process according to Claim 1, wherein:

the diastereomeric ratio of the product of (a), Compound of formula II, is at least
60%.

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23. A process according to Claim 22, wherein:

the diastereomeric ratio of the product of (a), Compound of formula II, is at least
80%.

24. A process according to Claim 3, wherein:

the diastereomeric ratio of the product of (c), Compound of formula IV, is at least 60%; and, the enantiomeric ratio of the product of (c), Compound of formula IV, is at least 60%.

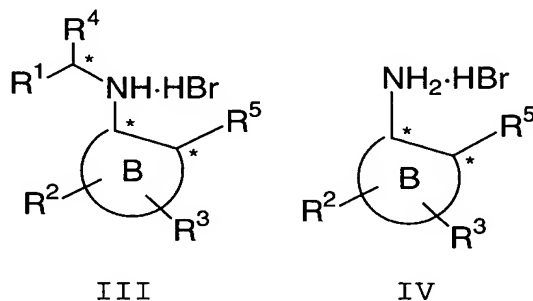
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25. A process according to Claim 24, wherein:

the diastereomeric ratio of the product of (c), Compound of formula IV, is at least 80%; and
the enantiomeric ratio of the product of (c), Compound of formula IV, is at least 80%.

10

26. A compound of formula III or IV:



15

wherein:

ring B is a 4-7 membered non-aromatic carbocyclic or heterocyclic ring consisting of: carbon atoms, 0-3 carbonyl groups, 0-3 double bonds, and 0-2 ring heteroatoms selected from O, N, NR⁶, and S(O)_p, provided that ring B contains other
than a S-S, O-O, or S-O bond;

20

R¹ is Q, -C₁₋₆ alkylene-Q, -C₂₋₆ alkenylene-Q, or -C₂₋₆ alkynylene-Q;

R² is Q, -C₁₋₆ alkylene-Q, -C₂₋₆ alkenylene-Q, -C₂₋₆ alkynylene-Q,
-(CR^aR^a1)_rO(CR^aR^a1)_s-Q, -(CR^aR^a1)_rNR^a(CR^aR^a1)_s-Q, -(CR^aR^a1)_rC(O)(CR^aR^a1)_s-Q,
-(CR^aR^a1)_rC(O)O(CR^aR^a1)_s-Q, -(CR^aR^a1)_rC(O)NR^aR^a1,
-(CR^aR^a1)_rC(O)NR^a(CR^aR^a1)_s-Q, -(CR^aR^a1)_rS(O)_p(CR^aR^a1)_s-Q, or
-(CR^aR^a1)_rSO₂NR^a(CR^aR^a1)_s-Q;

25

Q is, independently at each occurrence, H, a C₃₋₆ carbocycle substituted with 0-3 R^d, or a 5-10 membered heterocycle consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)_p, and substituted with 0-3 R^d;

R³ is H, Cl, F, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, -(CH)_r-phenyl substituted with 0-3 R^d, or -(CH)_r-5-6 membered heterocycle consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)_p, and substituted with 0-3 R^d;

alternatively, when R² and R³ are attached to the same carbon atom, they form a 3-8 membered carbocyclic or heterocyclic spiro ring C substituted with 0-2 R^c and consisting of carbon atoms, 0-4 heteroatoms selected from O, N, and S(O)_p, and 0-2 double bonds, provided that ring C contains other than a S-S, O-O, or S-O bond;

alternatively, when R² and R³ are attached to adjacent carbon atoms, together with the carbon atoms to which they are attached they form a 5-7 membered carbocyclic or heterocyclic ring D substituted with 0-2 R^c and consisting of carbon atoms, 0-2 heteroatoms selected from the group consisting of N, O, and S(O)_p, and 0-3 double bonds;

R⁴ is H, C₁₋₆ alkyl substituted with 0-1 R^b, C₂₋₆ alkenyl substituted with 0-1 R^b, or C₂₋₆ alkynyl substituted with 0-1 R^b;

R⁵ is -CH₂OR^a or -C(O)OR^a;

R⁶ is Q, -C₁₋₆ alkylene-Q, -C₂₋₆ alkenylene-Q, -C₂₋₆ alkynylene-Q, -(CR^aR^{a1})_rC(O)(CR^aR^{a1})_s-Q, -(CR^aR^{a1})_rC(O)-C₂₋₆ alkenylene-Q, -(CR^aR^{a1})_rC(O)O(CR^aR^{a1})_s-Q, -(CR^aR^{a1})_rC(O)NR^aR^{a1}, -(CR^aR^{a1})_rC(O)NR^a(CR^aR^{a1})_s-Q, -(CR^aR^{a1})_rS(O)_p(CR^aR^{a1})_s-Q, or -(CR^aR^{a1})_rSO₂NR^a(CR^aR^{a1})_s-Q;

R^a is, independently at each occurrence, H, C₁₋₆ alkyl, phenyl, or benzyl;

R^{a1} is, independently at each occurrence, H or C₁₋₆ alkyl;

R^{a2} is, independently at each occurrence, C₁₋₆ alkyl, phenyl, and benzyl;

R^b is, independently at each occurrence, C₁₋₆ alkyl substituted with 0-1 R^c, -OR^a, -SR^a, Cl, F, Br, I, =O, CN, NO₂, -NR^aR^{a1}, -C(O)R^a, -C(O)OR^a, -C(O)NR^aR^{a1}, -C(S)NR^aR^{a1}, -NR^aC(O)NR^aR^{a1}, -OC(O)NR^aR^{a1}, -NR^aC(O)OR^a, -S(O)₂NR^aR^{a1},

$-\text{NR}^{\text{a}}\text{S}(\text{O})_2\text{R}^{\text{a}2}$, $-\text{NR}^{\text{a}}\text{S}(\text{O})_2\text{NR}^{\text{a}}\text{R}^{\text{a}1}$, $-\text{OS}(\text{O})_2\text{NR}^{\text{a}}\text{R}^{\text{a}1}$, $-\text{S}(\text{O})_p\text{R}^{\text{a}2}$, CF_3 , $-\text{CF}_2\text{CF}_3$, $-\text{CHF}_2$, $-\text{CH}_2\text{F}$, or phenyl;

R^{c} is, independently at each occurrence, H , C_{1-4} alkyl, $-\text{OR}^{\text{a}}$, Cl , F , Br , I , $=\text{O}$, CF_3 , CN , NO_2 , $-\text{C}(\text{O})\text{R}^{\text{a}}$, $-\text{C}(\text{O})\text{OR}^{\text{a}}$, $-\text{C}(\text{O})\text{NR}^{\text{a}}\text{R}^{\text{a}}$, or $-\text{S}(\text{O})_p\text{R}^{\text{a}}$;

- 5 R^{d} is, independently at each occurrence, C_{1-6} alkyl, $-\text{OR}^{\text{a}}$, Cl , F , Br , I , $=\text{O}$, CN , NO_2 , $-\text{NR}^{\text{a}}\text{R}^{\text{a}1}$, $-\text{C}(\text{O})\text{R}^{\text{a}}$, $-\text{C}(\text{O})\text{OR}^{\text{a}}$, $-\text{C}(\text{O})\text{NR}^{\text{a}}\text{R}^{\text{a}1}$, $-\text{C}(\text{S})\text{NR}^{\text{a}}\text{R}^{\text{a}1}$, $-\text{NR}^{\text{a}}\text{C}(\text{O})\text{NR}^{\text{a}}\text{R}^{\text{a}1}$, $-\text{OC}(\text{O})\text{NR}^{\text{a}}\text{R}^{\text{a}1}$, $-\text{NR}^{\text{a}}\text{C}(\text{O})\text{OR}^{\text{a}}$, $-\text{S}(\text{O})_2\text{NR}^{\text{a}}\text{R}^{\text{a}1}$, $-\text{NR}^{\text{a}}\text{S}(\text{O})_2\text{R}^{\text{a}2}$, $-\text{NR}^{\text{a}}\text{S}(\text{O})_2\text{NR}^{\text{a}}\text{R}^{\text{a}1}$, $-\text{OS}(\text{O})_2\text{NR}^{\text{a}}\text{R}^{\text{a}1}$, $-\text{S}(\text{O})_p\text{R}^{\text{a}2}$, CF_3 , $-\text{CF}_2\text{CF}_3$, C_{3-10} carbocycle, or a 5-6 membered heterocycle consisting of: carbon atoms and 1-4 heteroatoms selected from the group
- 10 consisting of N , O , and $\text{S}(\text{O})_p$;

p , at each occurrence, is selected from 0, 1, and 2;

r , at each occurrence, is selected from 0, 1, 2, 3, and 4; and

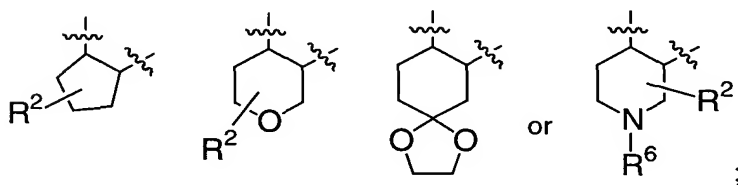
s , at each occurrence, is selected from 0, 1, 2, 3, and 4;

provided that ring B is other than cyclohexane.

15

27. A compound of formula III or IV, according to Claim 26, wherein:

ring B is:



- 20 R^1 is phenyl substituted with 0-3 R^{d} ;

R^2 is Q , $-\text{C}_{1-6}$ alkylene- Q , $-\text{C}_{2-4}$ alkenylene- Q , $-\text{C}_{2-4}$ alkynylene- Q , $-\text{C}(\text{O})(\text{CR}^{\text{a}}\text{R}^{\text{a}1})_s-\text{Q}$, $-\text{C}(\text{O})\text{O}(\text{CR}^{\text{a}}\text{R}^{\text{a}1})_s-\text{Q}$, $-\text{C}(\text{O})\text{NR}^{\text{a}}\text{R}^{\text{a}1}$, $-\text{C}(\text{O})\text{NR}^{\text{a}}(\text{CR}^{\text{a}}\text{R}^{\text{a}1})_s-\text{Q}$, $-\text{S}(\text{O})_p(\text{CR}^{\text{a}}\text{R}^{\text{a}1})_s-\text{Q}$, or $-\text{SO}_2\text{NR}^{\text{a}}(\text{CR}^{\text{a}}\text{R}^{\text{a}1})_s-\text{Q}$;

- Q is, independently at each occurrence, H , cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, tetrahydro-2H-pyran-4-yl, or phenyl substituted with 0-2 R^{d} ;
- 25

R^4 is C_{1-4} alkyl;

R^5 is $-\text{CH}_2\text{OR}^{\text{a}}$ or $-\text{C}(\text{O})\text{OR}^{\text{a}}$;

R^6 is Q , $-\text{C}_{1-6}$ alkylene- Q , $-\text{C}_{2-4}$ alkenylene- Q , $-\text{C}_{2-4}$ alkynylene- Q , $-\text{C}(\text{O})(\text{CR}^{\text{a}}\text{R}^{\text{a}1})_s-\text{Q}$, $-\text{C}(\text{O})\text{O}(\text{CR}^{\text{a}}\text{R}^{\text{a}1})_s-\text{Q}$, $-\text{C}(\text{O})\text{NR}^{\text{a}}\text{R}^{\text{a}1}$, $-\text{C}(\text{O})\text{NR}^{\text{a}}(\text{CR}^{\text{a}}\text{R}^{\text{a}1})_s-\text{Q}$,

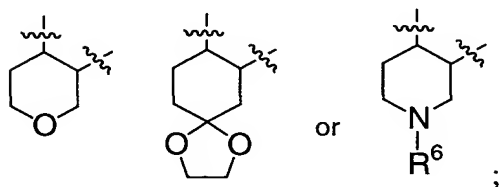
$-\text{S}(\text{O})_p(\text{CR}^a\text{R}^{a1})_s-\text{Q}$, or $-\text{SO}_2\text{NR}^a(\text{CR}^a\text{R}^{a1})_s-\text{Q}$; and

R^d is, independently at each occurrence, C_{1-6} alkyl, $-\text{OR}^a$, Cl , F , Br , $=\text{O}$, $-\text{NR}^a\text{R}^{a1}$, $-\text{C}(\text{O})\text{R}^a$, $-\text{C}(\text{O})\text{OR}^a$, $-\text{C}(\text{O})\text{NR}^a\text{R}^{a1}$, $-\text{S}(\text{O})_2\text{NR}^a\text{R}^{a1}$, $-\text{NR}^a\text{S}(\text{O})_2\text{R}^{a2}$, $-\text{S}(\text{O})_p\text{R}^{a2}$, CF_3 or phenyl.

5

28. A compound of formula III or IV, according to Claim 27, wherein:

ring B is:



10

R^1 is phenyl;

R^4 is C_{1-4} alkyl;

R^5 is $-\text{C}(\text{O})\text{OR}^a$;

15

R^6 is H, methyl, isopropyl, butyl, isobutyl, neopentyl, allyl, 3-butenyl, 2-propynyl, 2-butyryl, 3-butyryl, acetyl, t-butylcarbonyl, 4-pentenyl, t-butoxycarbonyl, methoxycarbonyl, methylsulfonyl, propylsulfonyl, isopropylsulfonyl, butylsulfonyl, phenyl, 4-F-phenyl, 4-methoxy-phenyl, cyclopropylmethyl, cyclopentyl, or tetrahydro-2H-pyran-4-yl; and

R^a is C_{1-4} alkyl.

20